PIGO gene

phosphatidylinositol glycan anchor biosynthesis class O

Normal Function

The *PIGO* gene provides instructions for making one part of an enzyme called GPI ethanolamine phosphate transfer 3 (GPI-ET3). The other part of the GPI-ET3 enzyme is produced from a gene called *PIGF*. The GPI-ET3 enzyme is involved in a series of steps that produce a molecule called a glycosylphosphosphatidylinositol (GPI) anchor. Specifically, this enzyme adds a molecule of ethanolamine phosphate to the end of the forming GPI anchor. This step takes place in the endoplasmic reticulum, which is a structure involved in protein processing and transport within cells. The complete GPI anchor attaches (binds) to various proteins in the endoplasmic reticulum; this process requires the ethanolamine phosphate at the end of the anchor. After the anchor and protein are bound, the anchor attaches itself to the outer surface of the cell membrane, ensuring that the protein will be available when it is needed.

Health Conditions Related to Genetic Changes

Mabry syndrome

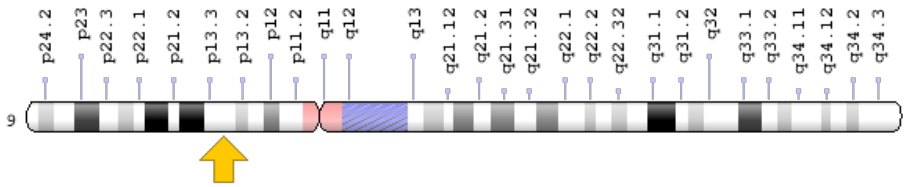
At least three mutations in the *PIGO* gene have been found to cause Mabry syndrome, a condition characterized by intellectual disability, distinctive facial features, increased levels of an enzyme called alkaline phosphatase in the blood (hyperphosphatasia), and other signs and symptoms. These mutations change single protein building blocks (amino acids) in the GPI-ET3 enzyme. The altered protein is less able to add ethanolamine phosphate to the end of GPI anchors. The incomplete GPI anchor cannot attach to proteins; without the anchor, the proteins cannot bind to the cell membrane and are released from the cell.

An enzyme called alkaline phosphatase is normally attached to the cell membrane by a GPI anchor. However, when the anchor is impaired, alkaline phosphatase is released from the cell. This abnormal release of alkaline phosphatase is responsible for the hyperphosphatasia in Mabry syndrome. It is unclear how *PIGO* gene mutations lead to the other features of Mabry syndrome, but these signs and symptoms are likely due to a lack of proper GPI anchoring of proteins to cell membranes.

Chromosomal Location

Cytogenetic Location: 9p13.3, which is the short (p) arm of chromosome 9 at position 13.3

Molecular Location: base pairs 35,085,493 to 35,096,601 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FLJ00135
- GPI ethanolamine phosphate transferase 3
- phosphatidylinositol glycan anchor biosynthesis, class O
- phosphatidylinositol-glycan biosynthesis class O protein
- PIG-O
- PIGO_HUMAN

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Glycosylphosphatidylinositol-Anchored Proteins (figure)
  https://www.ncbi.nlm.nih.gov/books/NBK28131/box/A206/
- Essentials of Glycobiology (second edition, 2009): Glycosylphosphatidylinositol Anchors
  https://www.ncbi.nlm.nih.gov/books/NBK1966/
- Molecular Biology of the Cell (fourth edition, 2002): The Attachment of a GPI Anchor to a Protein in the ER (figure)
  https://www.ncbi.nlm.nih.gov/books/NBK26841/figure/A2241/?report=objectonly

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PIGO%5BTIAB%5D%29+OR+%28PIG-O%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D

OMIM

- PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS O PROTEIN
  http://omim.org/entry/614730

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PIGO.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PIGO%5Bgene%5D
- HGNC Gene Family: Phosphatidylinositol glycan anchor biosynthesis
  http://www.genenames.org/cgi-bin/genefamilies/set/680
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=23215
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/84720
- UniProt
  http://www.uniprot.org/uniprot/Q8TEQ8

Sources for This Summary

- Hong Y, Maeda Y, Watanabe R, Inoue N, Ohishi K, Kinoshita T. Requirement of PIG-F and PIG-O for transferring phosphoethanolamine to the third mannose in glycosylphosphatidylinositol. J Biol Chem. 2000 Jul 7;275(27):20911-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10781593
- Krawitz PM, Murakami Y, Hecht J, Krüger U, Holder SE, Mortier GR, Delle Chiaie B, De Baere E, Thompson MD, Roscioli T, Kielbasa S, Kinoshita T, Mundlos S, Robinson PN, Horn D. Mutations in PIGO, a member of the GPI-anchor-synthesis pathway, cause hyperphosphatasia with mental retardation. Am J Hum Genet. 2012 Jul 13;91(1):146-51. doi: 10.1016/j.ajhg.2012.05.004. Epub 2012 Jun 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22683086
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397269/

- OMIM: PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS O PROTEIN
  http://omim.org/entry/614730
- Tsai YH, Liu X, Seeberger PH. Chemical biology of glycosylphosphatidylinositol anchors. Angew Chem Int Ed Engl. 2012 Nov 12;51(46):11438-56. doi: 10.1002/anie.201203912. Epub 2012 Oct 19. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23086912

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